REMARKS

Claims 1-11, 14-25, 28-35, 44, 45, and 69-74 are pending in the application. Claims 1, 3-5, 9, 11, 14-21, 29-35, 44, 45, and 71-74 have been amended. Claims 12, 13, 26, 27, 36-43, and 46-68 are provisionally cancelled without prejudice.

Claims 4 and 5 have been objected to under 37 CFR § 1.75(c) as being multiple dependent claims that are dependent on another multiple dependant claim. Claims 4 and 5, and non-objected to claim 3, are now amended to remove the multiple dependency reference.

Applicant notes and affirms the Examiner's renumbering of claims 25-74 in accord with 37 CFR § 1.126. Claims 29-35, 44, 45, and 71-74 have been renumbered to correct the dependencies of these claims in consequence of the renumbering.

Claims 1-3, 6-11, 14-35, 44-45, 69-74 are rejected under 35 U.S.C. §112, second paragraph, for being indefinite by not clearly defining what is meant by "catalytic domain GH48" or the specific function of such a peptide. Claim 1 has been amended to clarify that the GH48 catalytic domain is a catalytic domain classified in the glycoside hydrolase 48 family, for example, as recited in the specification on page 10 at lines 13-18 and the passage from page 15 at line 5 to page 16 at line 32.

Claims 26 and 27 have been cancelled because they refer to nucleic acid features that are not directly reflected in a transcribed amino acid product.

Claim 1, 2-3, 6-11, 14-35, 44-45, and 69-74 are rejected under 35 U.S.C. §112, second paragraph, as being indefinite for claiming a "substantially purified" thermostable

Gux1 peptide. The rejection is overcome by deleting the word "substantially." The term "purified" is described on page 12 of the specification, beginning at line 8.

Claim 11 is rejected under 35 U.S.C. §112, second paragraph, for indefiniteness due to recitation of a nucleotide sequence, when an amino acid sequence is claimed. This rejection is overcome by amending claim 11 to recite that the amino acid sequence is encoded by the nucleic acid sequence.

Claim 9 is rejected under 35 U.S.C. §112, second paragraph, for indefiniteness due to uncertainty whether all three sequence IDs are claimed. The rejection is overcome by reciting that the sequences are claimed in combination.

Claims 14-21 are rejected under 35 U.S.C. §112, second paragraph, for indefiniteness arising from whether an amino acid sequence or a polynucleotide sequence is claimed. These claims have been amended to clarify that the amino acid sequence is being claimed.

Claim 35 is rejected under 35 U.S.C. §112, second paragraph, for indefiniteness arising from a lack of antecedent for "the agent." Amended claim 35 now depends from claim 34, which provides a proper antecedent.

Claims 44-45 are rejected under 35 U.S.C. §112, second paragraph, for indefiniteness arising from the term "carrier." The Examiner states that it is unclear what type of carrier Applicant is claiming. Applicant respectfully traverses the rejection because many types of carriers are discussed in various contexts throughout the Specification, for example, on lines 28-30 on page 29, under the heading "Therapeutic Applications". The meaning of carrier is sufficiently clear, and Applicant should not have to amend.

Claims 1-3, 6-8, 22-25, 69-74 are rejected under 35 U.S.C. §112, first paragraph, as containing subject matter not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors had possession of the claimed invention. Applicant respectfully traverses this rejection and submits that it is well within the ordinary skill of the art to modify a polypeptide by at least one of deletion, addition, insertion and substitution of an amino acid residue. Techniques in molecular genetics for accomplishing deletion, addition, insertion and substitution of an amino acid residue are well-known, generally available techniques, for example, as mentioned in the passage beginning on page 20 at line 27 of the specification. "A patent need not teach, and preferably omits, what is well known in the art." *In re Buchern*, 929 F.2d 660, 661 (Fed. Cir. 1991).

Additionally, claims 1-3, 6-8, 22-25, 69-74 are rejected as the disclosure of a single species is insufficient to claim all species within the genus. It is error for the Examiner to assert, as a basis for this rejection, that "[t]he specification does not contain any disclosure of the structure of all the polypeptide sequences derived from SEQ ID NO. 1, including fragments and variants within the claimed scope of genus." That is not the requirement of law, and never has been, where in *Amgen Inc. v. Hoechst Marion Roussel Inc.*, 65 USPQ2d 1385 (CA FC 2003), the Court of Appeals for The Federal Circuit recently said:

> We move now to TKT's argument that Amgen failed to sufficiently describe all vertebrate and mammalian cells as engineered in the claimed invention. We held in *Eli Lilly* that the adequate description of claimed DNA requires a precise definition of the DNA sequence itself — not merely a recitation of its function or a reference to a potential method for isolating it. 119 F.3d at 1566-67, 43 USPQ2d at 1406 (holding the disclosure of the cDNA sequence of the insulin gene of a rat did not adequately describe the cDNA sequence of the insulin gene of every vertebrate). More recently, in *Enzo Biochem*, we clarified that *Eli Lilly* did not

> hold that all functional descriptions of genetic material necessarily fail as a matter of law to meet the written description requirement; rather, the requirement may be satisfied if in the knowledge of the art the disclosed function is sufficiently correlated to a particular, known structure. See *Enzo Biochem*, 296 F.3d at 1324, 63 USPQ2d at 1613.

Applicant has met the written description requirement for both species and genus by specifically and precisely reciting the nucleotide and amino acid sequences obtained from *A. celluloyticus*. Once these sequences became identified by virtue of Applicant's discovery, it also became easy to modify them on the basis of correlating the modifications to the particular, known structure that is precisely disclosed in this application. It is not necessary to disclose all of the possible modifications. It is sufficient that the modifications are correlated to the known structure that Applicant is claiming.

The Examiner has referred to "written description" guidelines published at www.uspto.gov and in the Official Gazette. We are unable to comment upon the specific guidelines referenced by the Examiner because they have not been specifically identified; however, any such guidelines will not withstand scrutiny to the extent that the guidelines depart from the requirements enunciated in *Amgen Inc.* and *Enzo Biochem*. Therefore, we respectfully traverse the §112 rejection of claims 1-3, 6-8, 22-25, 69-74 and request withdrawal of the rejection.

Claims 14-21 are rejected under 35 U.S.C. §112, first paragraph, as containing subject matter not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors had possession of the claimed invention. Specifically, Examiner claims that the specification does not disclose the function of all DNA sequences that are 70, 80, or 90% identical to SEQ ID NO: 1 or 4, 5, 6, 7.

Applicant respectfully disagrees that no disclosure is provided and references the specification where "...the invention is preferably at least about 60% identical, more preferably at least about 70% identical, or in some embodiments at least about 90 identical..." (page 18, line 39). The GH48, CBD II and CBDIII domains are well known families that are classified on the basis of function and structure (see, for example, the attached printout from the CAZy database). Therefore, it is error for Examiner to assert, on page 7 of the office action, that "many functionally unrelated DNAs are encompassed within the scope of these claims" when claim 1 recites the presence of GH48, CBD II and CBDIII domains. It is further error to assert that the written description fails to put one of skill in the art in possession of the species when these taxonomic classifications are fundamental aspects of skill in this art.

Claims 28-35, 44-45 are rejected under 35 U.S.C. §112, first paragraph, as containing subject matter not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors had possession of the claimed invention. Applicant respectfully traverses this rejection and submits that it is well within the ordinary skill of the art to modify a polypeptide by at least one of deletion, addition, insertion and substitution of an amino acid residue. Techniques in molecular genetics for accomplishing deletion, addition, insertion and substitution of an amino acid residues are well-known, generally available techniques, for example, as mentioned in the passage beginning on page 20 at line 27 of the specification. "A patent need not teach, and preferably omits, what is well known in the art." *In re Buchern*, 929 F.2d 660, 661 (Fed. Cir. 1991).

Claims 1-3, 6-10, 14-25, 28-35, 44-45, 69-74 are rejected under 35 U.S.C. §103(a) as being unpatentable over Zverlov et al and Tomme et al. Zverlov et al. is applied to show a GH48 domain linked to a CBDIII domain, but lacks an additional CBDII domain. Tomme et al. is used to show a comparison between different CBDs, and is applied for the purpose of showing that type II and type III domains bind irreversibly, which may be a favorable type of binding for some applications. Tomme et al,. is also said to teach the manipulation of CBDs and their sources.

The rejection does not establish a prima facie case of obviousness because there is no motivation to combine the references in a manner that teaches a GH48 domain linked to both a CBDIII and CBDII domain. If one skilled in the art were to follow the combined teaching, the CBDIII of Zverlov et al. might be replaced by the CBDII of Tomme et al.. The references provide no motivation for linking both CBDII and CBDIII to GH48. The fact that Applicant has discovered the linked GH48, CBDIII and CBDII domains in nature presumptively establishes the fact that *A. celluolyticus* evolved to contain a combination of CBDs and with the GH48 domain, and the organism did so for a reason. The Examiner has merely shown that a GH48 domain exists in combination with CBDIII. Also shown is that CBDIII and CBDII domains are known. What is not suggested by the references is any reason why GH48, CBDIII and CBDII should be linked in combination.

We emphatically disagree with the bald assertion, on page 11 of the office action, that "[s]uch construction of hybrid cellulose [cellulase?] is well known in the art." There is no reference showing that GH48 should be combined with both CBDIII and CBDII. The Examiner appears to argue that the additional CBD would be desirable because it

would make the cellulose-cellulase binding interaction more robust. That is mere hindsight speculation and, further, the alleged motivation is self-contradictory. First off, if both the CBDIII and CBDII interactions are irreversible, as argued by the Examiner, there would be no reason to make the binding interaction more robust. Secondly, until both binding domains were observed in nature, as reported in the present specification, there was never any reason to expect that a particular organism evolved to have the special advantage of the two CBDs linked to a GH48 domain. Therefore, the claimed invention cannot be obvious in view of Zverlov et al. and Tomme et al. because there is no motivation to combine.

Even if Zverlov et al. and Tomme et al. are indiscriminately combined despite lack of any motivation, they still fail to teach or suggest the limitations of claim 1. Nothing in the combination of references teaches or suggests combining GH48 with CBDIII and CBDII domains. The Examiner argues that one skilled in the art may "pick and choose" from among all CBDs. Assuming, arguendo, that were done, the CBDIII of Zverlov et al. might be substituted with CBDII, but not a combination including GH48, CBDIII and CBDII as is presently claimed.

The Examiner attempts to impose a burden on Applicant to show patentable structural differences or unobvious advantages over the "prior art." At this time, the burden is improperly shifted to Applicant because the Examiner has not established a prima facie case. Unexpected advantage is demonstrated by the fact that *A. celluloyticus* has evolved to excrete a cellulase having the claimed structure.

Applicant further notes that none of the articles cited against the claims describes the sequences specifically claimed in Applicant's claims 6-11, 14-21, 28, and 33. The articles are completely silent as to these sequences.

Applicant's attorney respectfully solicits a Notice of Allowance in this application. The Commissioner is authorized to charge any additionally required fees to deposit account 14-0460. Should the Examiner have any questions, comments, or suggestions that would expedite the prosecution of the present case to allowance, Applicants' representative, Paul White, earnestly requests a telephone call at (303) 384-7575.

Respectfully submitted

Paul J. White 5/28/03

Paul J. White, Reg. No. 30,436
Senior Patent Counsel
National Renewable Energy Laboratory
1617 Cole Boulevard
Golden, CO. 80401
(303) 384-7575